SEQUENCE LISTING

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<110> Johnson, Jeffrey D.
      Palma, John F.
      Schweitzer, Anthony C.
      Blume, John E.
     Metabolex, Inc.
<120> A Pancreatic Islet Transcription Factor and Uses
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<140> US 10/533,593
<141> 2005-05-02
<150> US 60/425,968
<151> 2002-11-13
<150> WO PCT/US03/36131
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Leu Gly Lys Gly Leu Leu Val Tyr Pro Glu Glu Thr Val Tyr Leu Ala
Ala Glu Gly Gln Pro Gly Gly Glu Gln Gly Gly Glu Lys Gly Glu
Asp Pro Glu Leu Pro Gly Ala Val Lys Ser Glu Met His Leu Asn Asn
Gly Asn Phe Ser Ser Glu Glu Glu Asp Ala Asp Asn His Asp Ser Lys
Thr Lys Ala Ala Asp Gln Tyr Leu Ser Gln Lys Lys Thr Ile Thr Gln
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Arg Lys Gln Thr Ser Ser Phe Tyr Thr Asp Thr Ser Ser Pro Val Ala

Arg Lys Gin Thr Ser Ser Phe Tyr Thr Asp Thr Ser Ser Pro Val Ala 850 860

Cys Arg Thr Pro Val Leu Ala Ser Ser Leu Gln Thr Pro Ile Pro Ser 865 870 875 880

Ser Ser Ser Gln Cys Met Tyr Gly Thr Ser Asn Gln Tyr Pro Ala Gln 885 890 895

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Gly Xaa Xaa Xaa Ser Glu Xaa Xaa Xaa Xaa Xaa His Xaa Ser Xaa 85 90 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Lys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Lys Xaa Xaa Xaa Thr Xaa Xaa Thr Leu Gln Trp Leu Glu Glu Asn Tyr Xaa Xaa Xaa Glu Gly Val Cys Leu Pro Arg Cys Xaa Leu Tyr Xaa His Tyr Leu Asp Phe Cys Xaa Lys Xaa Xaa Xaa Pro Xaa Xaa Ala Ala Xaa Phe Gly Lys Xaa Ile Arg Gln Xaa Phe Pro Xaa 170 Leu Thr Thr Arg Arg Leu Gly Thr Arg Gly Xaa Ser Lys Tyr His Tyr Tyr Gly Ile Xaa Xaa Lys Glu Ser Ser Xaa Tyr Tyr Xaa Xaa Xaa Tyr Ser Xaa Lys Gly Xaa Xaa Xaa Xaa Ser Xaa Xaa Xaa Lys Xaa Xaa 215 Xaa Xaa Xaa Thr Xaa Xaa Tyr Ser Xaa Xaa Ser Lys Xaa Gly Thr Leu Leu Pro Glu Phe Pro Xaa Xaa Gln His Xaa Xaa Xaa Xaa Xaa Ile 245 250 Xaa Xaa Xaa Lys Val Xaa Thr Leu Ile Met Met Tyr Xaa Thr His Cys 265 Gln Xaa Ile Leu Asp Xaa Xaa Ile Xaa Xaa Asn Phe Xaa Glu Xaa Gln Xaa Phe Leu His Phe Trp Gln Gly Met Pro Asp His Xaa Leu Pro Leu Xaa Xaa Xaa Xaa Xaa Xaa Asp Ile Xaa Xaa Val Cys Asp Ser 315 Ile Leu Tyr Lys Xaa Xaa Xaa Asp Val Leu Ile Pro Xaa Xaa Kaa Gln Glu Xaa Pro Xaa Ser Leu Xaa Xaa Xaa Ile Arg Xaa Phe Ala Lys Asn Xaa Xaa Xaa Trp Xaa Xaa Xaa Ser Leu Xaa Asn Leu Pro Glu Xaa Leu 360 Xaa Xaa Lys Lys Ile Xaa Xaa Xaa Arg Arg Phe Xaa Xaa Xaa Leu Lys 375 Arg Gln Thr Ser Xaa Xaa His Leu Ala Gln Xaa Xaa Arg Xaa Xaa Leu 390 395

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Asp	Xaa 530	Tyr	Xaa	Leu	Xaa	Xaa 535	Xaa	Glu	Xaa	Xaa	Xaa 540	Xaa	Xaa	Xaa	Xaa
Xaa 545	Gln	Glu	Xaa	Xaa	Asn 550	Xaa	Leu	Xaa	Xaa	Xaa 555	Met	Lys	Xaa	Xaa	Xaa 560
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725 730 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Ser Pro Xaa Xaa Xaa 745 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Leu Ser Asn Thr Gly 775 780 795 790 805 810 820 825 885 890 905 910 915 920 925 <210> 4 <211> 75 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: RFX DNA binding domain (DBD) consensus sequence <220> <221> MOD RES <222> (1)..(75) <223> Xaa = any amino acid <400> 4 Thr Leu Gln Trp Leu Xaa Xaa Asn Tyr Xaa Xaa Xaa Glu Gly Val Xaa

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Xaa Xaa Trp Xaa Xaa Xaa Leu

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            20
Ser Asp Xaa Xaa Arg Val Asp Xaa Asn Xaa Xaa Xaa Gln Ala Xaa
50
                       55
Xaa Xaa Xaa Xaa Xaa Xaa Gln Xaa Xaa Lys Xaa Xaa Leu Xaa Xaa
Xaa Xaa Xaa Glu Xaa Xaa Glu Trp Leu Asp Xaa Val Xaa Xaa
                                  90
Gln Xaa Xaa Xaa Xaa Xaa Xaa Tyr Xaa Xaa Xaa Xaa Xaa Xaa Lys
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Xaa Ala Xaa Xaa Phe Leu Leu Lys Trp Ser Phe Xaa Xaa Xaa Xaa Val
                          120
Xaa Xaa Xaa Leu Thr Leu Xaa Xaa Ala Xaa Ser Phe Gly Ser Phe His
Leu Ile Arg Xaa Leu Xaa Asp Glu Tyr Xaa Xaa Xaa Xaa Xaa Glu Xaa
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Leu Pro Arg Cys Ile Leu Tyr Ala His Tyr Leu Asp Phe Cys Arg Lys 25 Glu Lys Leu Glu Pro Ala Cys Ala Ala Thr Phe Gly Lys Thr Ile Arg Gln Lys Phe Pro Leu Leu Thr Thr Arg Arg Leu Gly Thr Arg Gly His Ser Lys Tyr His Tyr Tyr Gly Ile Gly Ile Lys Glu 70 <210> 9 <211> 36 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: exemplary RFX B <400> 9 Lys Val Asp Thr Leu Ile Met Met Tyr Lys Thr His Cys Gln Cys Ile Leu Asp Asn Ala Ile Asn Gly Asn Phe Glu Glu Ile Gln His Phe Leu 25 Leu His Phe Trp 35 <210> 10 <211> 40 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: exemplary RFX C domain <400> 10 Leu Tyr Lys Val Leu Thr Asp Val Leu Ile Pro Ala Thr Met Gln Glu Met Pro Glu Ser Leu Leu Ala Asp Ile Arg Asn Phe Ala Lys Asn Trp 25 Glu Gln Trp Val Val Ser Ser Leu 35 <210> 11 <211> 179 <212> PRT <213> Artificial Sequence

<223> Description of Artificial Sequence: exemplary RFX

dimerization domain

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Gln Ile Ala Arg Pro Ala Leu Phe Asp Gln His Val Val Asn Ser Met
20 25 30

Val Ser Asp Ile Glu Arg Val Asp Leu Asn Ser Ile Gly Ser Gln Ala 35 40 45

Leu Leu Thr Ile Ser Gly Ser Thr Asp Thr Glu Ser Gly Ile Tyr Thr 50 60

Glu His Asp Ser Ile Thr Val Phe Gln Glu Leu Lys Asp Leu Leu Lys 65 70 75 80

Lys Asn Ala Thr Val Glu Ala Phe Ile Glu Trp Leu Asp Thr Val Val 85 90 95

Glu Gln Arg Val Ile Lys Thr Ser Lys Gln Asn Gly Arg Ser Leu Lys 100 105 110

Lys Arg Ala Gln Asp Phe Leu Leu Lys Trp Ser Phe Phe Gly Ala Arg
115 120 125

Val Met His Asn Leu Thr Leu Asn Asn Ala Ser Ser Phe Gly Ser Phe 130 135 140

His Leu Ile Arg Met Leu Leu Asp Glu Tyr Ile Leu Leu Ala Met Glu 145 150 155 160

Thr Gln Phe Asn Asn Asp Lys Glu Gln Glu Leu Gln Asn Leu Leu Asp
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Lys Tyr Met

<210> 12

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<212> PRT

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1 10 15

Ile Pro Arg Ser Ala Leu Tyr Met His Tyr Leu Asp Phe Cys Glu Lys

Asn Asp Thr Gln Pro Val Asn Ala Ala Ser Phe Gly Lys Ile Ile Arg
35 40 45

Gln Gln Phe Pro Gln Leu Thr Thr Arg Arg Leu Gly Thr Arg Gly Gln
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Ser Lys Tyr His Tyr Tyr Gly Ile Ala Val Lys Glu 65 70 75

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<211> 77

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<223> Description of Artificial Sequence:RFX5 DNA binding domain

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Leu Ala Cys Cys Arg Pro Leu Ser Thr Ala Asn Phe Gly Lys Ile Ile 35 40 45

Arg Glu Ile Phe Pro Asp Ile Lys Ala Arg Arg Leu Gly Gly Arg Gly 50 55 60

Gln Ser Lys Tyr Cys Tyr Ser Gly Ile Arg Arg Lys Thr
65 70 75

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<211> 75

<212> PRT

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1 5 10 15

Pro Arg Cys Glu Leu Tyr Asp His Tyr Lys Lys His Cys Ala Glu His

Arg Met Asp Pro Val Asn Ala Ala Ser Phe Gly Lys Leu Ile Arg Ser 35 40 45

Val Phe His Asn Leu Lys Thr Arg Arg Leu Gly Thr Arg Gly Asn Ser 50 55 . 60

Lys Tyr His Tyr Tyr Gly Ile Arg Leu Lys Asp
65 70 75

<210> 15

<211> 76

<212> PRT

<213> Artificial Sequence

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Leu Pro Arg Ser Thr Leu Tyr Asn His Tyr Leu Arg His Cys Gln Glu
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His Lys Leu Asp Pro Val Asn Ala Ala Ser Phe Gly Lys Leu Ile Arg
35 40 45

Ser Ile Phe Met Gly Leu Arg Thr Arg Arg Leu Gly Thr Arg Gly Asn 50 55 60

Ser Lys Tyr His Tyr Tyr Gly Ile Arg Val Lys Pro 65 70 75

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<211> 76

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Leu Pro Arg Ser Ser Leu Tyr Asn His Tyr Leu Arg His Cys Gln Glu 20 25 30

His Lys Leu Asp Pro Val Asn Ala Ala Ser Phe Gly Lys Leu Ile Arg
35 40 45

Ser Val Phe Met Gly Leu Arg Thr Arg Arg Leu Gly Thr Arg Gly Asn 50 55 60

Ser Lys Tyr His Tyr Tyr Gly Ile Arg Leu Lys Pro 65 70 75

<210> 17

<211> 76

<212> PRT

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1 10 15

Leu Pro Arg Ser Thr Leu Tyr Cys His Tyr Leu Leu His Cys Gln Glu 20 25 30

Gln Lys Leu Glu Pro Val Asn Ala Ala Ser Phe Gly Lys Leu Ile Arg $35 \hspace{1cm} 40 \hspace{1cm} 45$

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<400> 19
Ala Glu Gly Val Ser Leu Pro Arg Ser
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Ile Arg
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Leu Ala Leu Ile Lys Asn Ile Asp Phe Ala Ser Val Glu Asp Thr Trp
Ser Lys Phe Trp
         35
<210> 23
<211> 36
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<223> Description of Artificial Sequence: RFX1 B domain
<400> 23
Asp Ile Lys Ala Phe Gln Val Leu Tyr Arg Glu His Cys Glu Ala Ile
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Val Asp Val Met Val Asn Leu Gln Phe Thr Leu Val Glu Thr Leu Trp
Lys Thr Phe Trp
         35
<210> 24
<211> 36
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: RFX2 B domain
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Asp Val Lys Ala Leu Gln Leu Val Tyr Arg Arg His Cys Glu Ala Thr
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Val Asp Val Val Met Asn Leu Gln Phe His Tyr Ile Glu Lys Leu Trp 20 25 Leu Ser Phe Trp 35 <210> 25 <211> 36 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: RFX4 B domain <400> 25 Lys Val Ser Thr Phe Ile Met Met Tyr Arg Thr His Cys Gln Arg Ile Leu Asp Thr Val Ile Arg Ala Asn Phe Asp Glu Val Gln Ser Phe Leu Leu His Phe Trp 35 <210> 26 <211> 36 <212> PRT <213> Artificial Sequence <223> Description of Artificial Sequence: RFX3 B domain Asp Ile Lys Ser Leu Gln Ser Leu Tyr Arg Glu His Cys Glu Ala Ile Leu Asp Val Val Val Asn Leu Gln Phe Ser Leu Ile Glu Lys Leu Trp Gln Thr Phe Trp <210> 27 <211> 40 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: RFX4 C domain <400> 27 Leu Tyr Lys Ala Ile Ser Gly Val Leu Met Pro Thr Val Leu Gln Ala

10

Leu Pro Asp Ser Leu Thr Gln Val Ile Arg Lys Phe Ala Lys Gln Leu 25 Asp Glu Trp Leu Lys Val Ala Leu <210> 28 <211> 40 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: RFX1 C domain <400> 28 Leu Tyr Gln Gly Leu Val Glu Ile Leu Ile Pro Asp Val Leu Arg Pro 5 Ile Pro Ser Ala Leu Thr Gln Ala Ile Arg Asn Phe Ala Lys Ser Leu Glu Ser Trp Leu Thr His Ala Met 35 <210> 29 <211> 41 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: C. elegans RFX protein daf-19 C domain <400> 29 Leu Tyr Gln Thr Ile Val Asp Thr Leu Ile Pro Asn Val Leu Leu Ser 1 5 Glu Leu Ser Thr Gly Met Thr Gln Thr Cys Arg Thr Phe Ala Lys Asn Ile Asp Val Tyr Leu Arg Lys Ser Leu 35 <210> 30 <211> 174 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: RFX4 dimerization domain <400> 30 Arg Phe Ser Gln Ile Leu Arg Arg Gln Thr Ser Leu Asn His Leu Cys 10

Gln Ala Ser Arg Thr Val Ile His Ser Ala Asp Ile Thr Phe Gln Met

25

20

- Leu Glu Asp Trp Arg Asn Val Asp Leu Asn Ser Ile Thr Lys Gln Thr 35 40 45
- Leu Tyr Thr Met Glu Asp Ser Arg Asp Glu His Arg Lys Leu Ile Thr 50 55 60
- Gln Leu Tyr Gln Glu Phe Asp His Leu Leu Glu Glu Gln Ser Pro Ile 65 70 75 80
- Glu Ser Tyr Ile Glu Trp Leu Asp Thr Met Val Asp Arg Cys Val Val 85 90 95
- Lys Val Ala Ala Lys Arg Gln Gly Ser Leu Lys Lys Val Ala Gln Gln
 100 105 110
- Phe Leu Leu Met Trp Ser Cys Phe Gly Thr Arg Val Ile Arg Asp Met 115 120 125
- Thr Leu His Ser Ala Pro Ser Phe Gly Ser Phe His Leu Ile His Leu 130 135 140
- Met Phe Asp Asp Tyr Val Leu Tyr Leu Leu Glu Ser Leu His Cys Gln 145 150 155 160
- Glu Arg Ala Asn Glu Leu Met Arg Ala Met Lys Gly Glu Gly
 165 170
- <210> 31
- <211> 170
- <212> PRT
- <213> Artificial Sequence
- <220>
- <223> Description of Artificial Sequence:C. elegans RFX protein daf-19 dimerization domain
- <400> 31
- Tyr Leu Gln Gln Gly Leu Lys Arg Tyr Thr Ser Leu Asn His Leu Ala 1 5 10 15
- His Ala Ser Arg Gly Val Leu Met Lys Pro Glu Gln Val Gln Gln Met
 20 25 30
- Tyr Gln Asp Tyr Ile Arg Val Asp Ile Asn Thr Val His Gln Gln Ala 35 40 45
- Gly Trp Ile Cys Gly Cys Asp Ser Val Met Val His His Val Asn Asn 50 55 60
- Ala Phe Lys His Asn Leu Gln Arg Met Ser Ala Met Glu Val Trp Ala 65 70 75 80
- Glu Trp Leu Glu Ser Ile Val Asp Gln Val Leu Ala Lys Tyr His Asp 90 95
- Lys Pro Ala Asn Val Ile Ala Asn Val Gly Lys Gln Phe Leu Leu Asn 100 105 110
- Trp Ser Phe Tyr Thr Ser Met Ile Ile Arg Asp Leu Thr Leu Arg Ser 115 120 125

Ala Met Ser Phe Gly Ser Phe Thr Leu Ile Arg Leu Leu Ala Asp Asp 130 135 140

Tyr Met Tyr Tyr Leu Ile Glu Ser Lys Ile Ala Lys Ala Gly Lys Gln 145 150 155 160

Gln Leu Ile Thr Val Ile Arg Ala Asp Lys 165 170

<210> 32

<211> 168

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:RFX3
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<400> 32

Ala Phe Ala Gln Thr Leu Arg Arg Tyr Thr Ser Leu Asn His Leu Ala 1 5 10 15

Gln Ala Ala Arg Ala Val Leu Gln Asn Thr Ser Gln Ile Asn Gln Met 20 25 30

Leu Ser Asp Leu Asn Arg Val Asp Phe Ala Asn Val Gln Glu Gln Ala 35 40 45

Ser Trp Val Cys Gln Cys Asp Asp Asn Met Val Gln Arg Leu Glu Thr 50 55 60

Asp Phe Lys Met Thr Leu Gln Gln Gln Ser Thr Leu Glu Gln Trp Ala 65 70 75 80

Ala Trp Leu Asp Asn Val Met Met Gln Ala Leu Lys Pro Tyr Glu Gly
85 90 95

Arg Pro Ser Phe Pro Lys Ala Ala Arg Gln Phe Leu Leu Lys Trp Ser 100 105 110

Phe Tyr Ser Ser Met Val Ile Arg Asp Leu Thr Leu Arg Ser Ala Ala 115 120 125

Ser Phe Gly Ser Phe His Leu Ile Arg Leu Leu Tyr Asp Glu Tyr Met 130 140

Phe Tyr Leu Val Glu His Arg Val Ala Gln Ala Thr Gly Glu Thr Pro 145 150 155 160

Ile Ala Val Met Gly Glu Val Arg 165

<210> 33

<211> 168

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:RFX1 dimerization domain

<400> 33

Ala Phe Ala Gln Thr Leu Arg Arg Tyr Thr Ser Leu Asn His Leu Ala 1 5 10 15

Gln Ala Arg Ala Val Leu Gln Asn Thr Ala Gln Ile Asn Gln Met
20 25 30

Leu Ser Asp Leu Asn Arg Val Asp Phe Ala Asn Val Gln Glu Gln Ala
35 40 45

Ser Trp Val Cys Arg Cys Glu Asp Arg Val Val Gln Arg Leu Glu Gln 50 55 60

Asp Phe Lys Val Thr Leu Gln Gln Gln Asn Ser Leu Glu Gln Trp Ala 65 70 75 80

Ala Trp Leu Asp Gly Val Val Ser Gln Val Leu Lys Pro Tyr Gln Gly 85 90 95

Ser Ala Gly Phe Pro Lys Ala Ala Lys Leu Phe Leu Lys Trp Ser 100 105 110

Phe Tyr Ser Ser Met Val Ile Arg Asp Leu Thr Leu Arg Ser Ala Ala 115 120 125

Ser Phe Gly Ser Phe His Leu Ile Arg Leu Leu Tyr Asp Glu Tyr Met 130 135 140

Tyr Tyr Leu Ile Glu His Arg Val Ala Gln Ala Lys Gly Glu Thr Pro 145 150 155 160

Ile Ala Val Met Gly Glu Phe Ala 165

<210> 34

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:RFX dimerization domain consensus sequence

<400> 34

Leu Arg Arg Tyr Thr Ser Leu Asn His Leu Ala Gln Ala Ala Arg
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<210> 35

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:RFX dimerization domain consensus sequence

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Asn Gln Met Leu Ser Asp
<210> 36
<211> 6
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<400> 36
Trp Ala Glu Trp Leu Asp
<210> 37
<211> 9
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:RFX
      dimerization domain consensus sequence
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Gln Phe Leu Leu Lys Trp Ser Phe Tyr
  1
<210> 38
<211> 12
<212> PRT
<213> Artificial Sequence
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Ser Met Val Ile Arg Asp Leu Thr Leu Arg Ser Ala
<210> 39
<211> 11
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence:RFX
      dimerization domain consensus sequence
<400> 39
Ser Phe Gly Ser Phe His Leu Ile Arg Leu Leu
                 5
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7 y e

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<210> 40
<211> 4
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence:RFX
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<400> 40
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<210> 41
<211> 6
<212> PRT
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<400> 41
His His His His His
<210> 42
<211> 200
<212> PRT
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<223> Description of Artificial Sequence:poly-Gly
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<220>
<221> MOD RES
<222> (6)..(200)
<223> Gly residues from position 6 to 200 may be present
   or absent
<400> 42
85
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185

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Gly Gly Gly Gly Gly Gly Gly 195 200